

CONCLUSION

The claims have been amended to clarify the invention and are clearly free of the art. It is believed that the pending claims are in a position for allowance and passage of claims 1-6, 9, 16-42 and 45-70 to issue is respectfully requested.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. **219002029000**.

Respectfully submitted,

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EXHIBIT A. - VERSION WITH MARKINGS TO SHOW CHANGES MADE

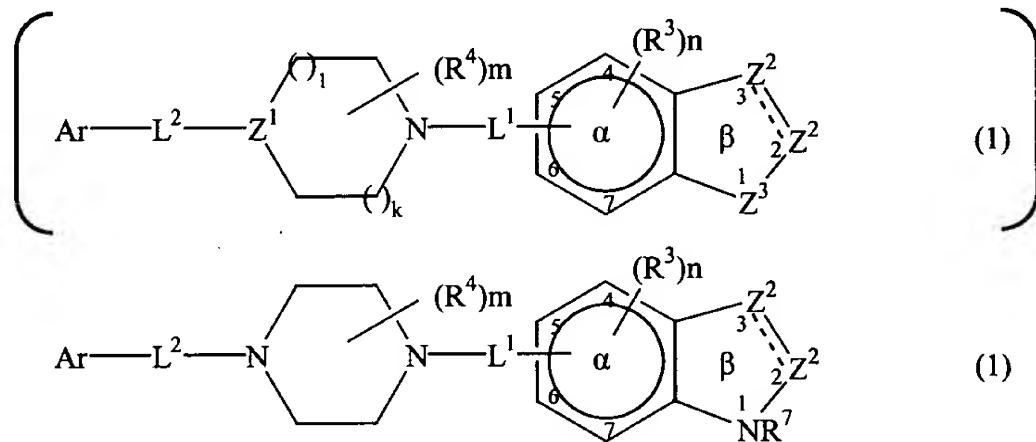
In the Specification:

In the paragraph on page 10, line 26 to page 11, line 3, modify as follows:

A is $-W_i-COX_jY$ wherein Y is COR^2 or an isostere thereof and R^2 is a noninterfering substituent. Each of W and X is a spacer and may be, for example, optionally substituted [alkyl, alkenyl, or alkynyl] alkylene, alkenylene, or alkynylene, each of i and j is 0 or 1. Preferably, W and X are unsubstituted. Preferably, j is 0 so that the two carbonyl groups are adjacent to each other. Preferably, also, i is 0 so that the proximal CO is adjacent the ring. However, compounds wherein the proximal CO is spaced from the ring can readily be prepared by selective reduction of an initially glyoxal substituted β ring. In the most preferred embodiments of the invention, the α/β ring system is an indole containing CA in position 3- and wherein A is $[COCR^2] COCOR^2$.

In the Claims:

1. (Twice amended) A compound of the formula:



and the pharmaceutically acceptable salts thereof, or a pharmaceutical composition thereof, wherein



represents a single or double bond;

one Z^2 is CA or CR^8A and the other is CR^1 , CR^1_2 , NR^6 or N wherein each R^1 , R^6 and R^8 is independently hydrogen or noninterfering substituent;

A is $-W_i-COX_jY$ wherein Y is COR² or an isostere thereof and R² is hydrogen or a noninterfering substituent, each of W and X is a spacer of 2-6 Å which is substituted or unsubstituted alkylene, alkenylene or alkynylene, and each of i and j is independently 0 or 1;

[Z³ is NR⁷ or O;]

R⁷ is H or is optionally substituted alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, heteroalkyl, heteroalkenyl, heteroalkynyl, heteroalkylaryl, or is SOR, SO₂R, RCO, COOR, alkyl-COR, SO₃R, CONR₂, SO₂NR₂, CN, CF₃, NR₂, OR, alkyl-SR, alkyl-SOR, alkyl-SO₂R, alkyl-OCOR, alkyl-COOR, alkyl-CN, alkyl-CONR₂, or R₃Si, wherein each R is independently H, alkyl, alkenyl or aryl or heteroforms thereof;

each R³ is independently a noninterfering substituent;

n is 0-3;

each of L¹ and L² is [a linker] independently alkylene (1-4C) or alkenylene (1-4C) optionally substituted with a moiety selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, heteroalkyl, heteroalkenyl, heteroalkynyl, heteroalkylaryl, NH-royl, halo, OR, NR₂, SR, SOR, SO₂R, OCOR, NRCOR, NRCONR₂, NRCOOR, OCONR₂, RCO, COOR, alkyl-OOR, SO₃R, CONR₂, SO₂NR₂, NRSO₂NR₂, CN, CF₃, R₃Si, and NO₂, wherein each R is independently H, alkyl, alkenyl or aryl or heteroforms thereof, and wherein two substituents on L¹ or L² can be joined to form a non-aromatic saturated or unsaturated ring that includes 0-3 heteroatoms which are O, S and/or N and which contains 3 to 8 members or said two substituents can be joined to form a carbonyl moiety or an oxime, oximeether, oximeester or ketal of said carbonyl moiety;

each R⁴ is independently a noninterfering substituent;

m is 0-4;

[Z¹ is N;

each of l and k is 1;]

Ar is an aryl group substituted with 0-5 noninterfering substituents, wherein two noninterfering substituents can form a fused ring; and

the distance between the atom of Ar linked to L² and the center of the α ring is 4.5-24 Å.

9. (Amended) The compound of claim [8] 1 wherein R⁷ is H, or is optionally substituted alkyl, or acyl.

16. (Amended) The compound of claim [15] 1 wherein L^2 is unsubstituted alkylene and L^1 is CO.

17. (Amended) The compound of claim [15] 1 wherein L^2 is unsubstituted methylene, methylene substituted with alkyl, or $-CH=$ and L^1 is alkylene or CO.

30. (Amended) The compound of claim 1 wherein Z^2 at position 3 is CA or $[CH^1A]$ CHA.